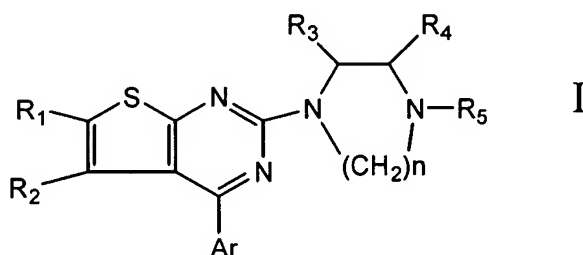


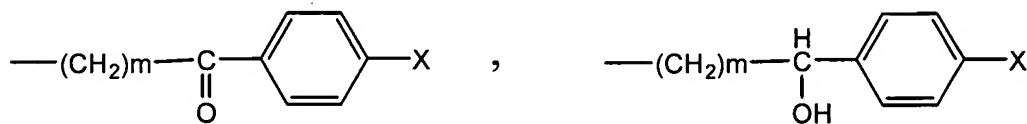
## CLAIMS

What is claimed is:

1. A method of treating nausea, vomiting, retching or any combination thereof in a  
 5 subject in need thereof comprising administering to said subject a therapeutically effective amount of a compound of Formula I:



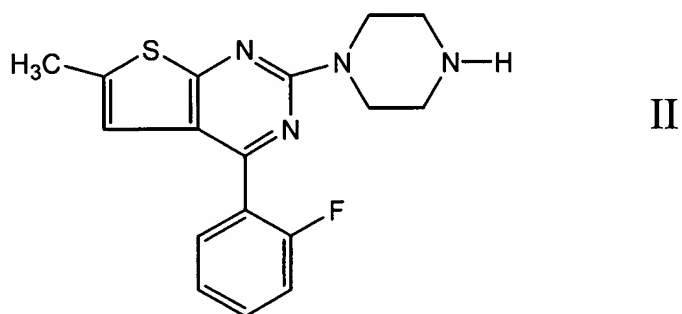
- wherein,  $R_1$  and  $R_2$  independently represent hydrogen, halogen or a  $C_1$ - $C_6$  alkyl  
 10 group; or  $R_1$  and  $R_2$  together with the carbon atom to which they are attached form a cycloalkylene group having 5 to 6 carbon atoms;  
 $R_3$  and  $R_4$  independently represent hydrogen or a  $C_1$ - $C_6$  alkyl group;  
 $R_5$  is hydrogen,  $C_1$ - $C_6$  alkyl,



- 15 or  $-C(O)-NH-R_6$   
 wherein  $m$  is an integer from about 1 to about 3,  $X$  is halogen and  $R_6$  is a  $C_1$ - $C_6$  alkyl group; and  
 $Ar$  is a substituted or unsubstituted phenyl, 2-thienyl or 3-thienyl group; and  
 $n$  is 2 or 3; or a pharmaceutically acceptable salt thereof.

2. The method of Claim 1, wherein the the nausea, vomiting, retching or any combination thereof is caused by an anesthetic, radiation, a cancer chemotherapeutic agent, a toxic agent, an odor, a medicine, pregnancy or motion.
- 5 3. The method of Claim 2, wherein the medicine is selected from the group consisting of an analgesic, an antibiotic, an antifungal or a serotonin reuptake inhibitor.
4. The method of Claim 1, wherein the nausea, vomiting, retching or any combination thereof is caused by a condition which is associated with vertigo.
- 10 5. The method of Claim 1, wherein the nausea, vomiting, retching or any combination thereof is caused by headache.
6. The method of Claim 1, wherein the nausea, vomiting, retching or any combination thereof is caused by a malady of the gastrointestinal (GI) tract.
7. The method of Claim 1, wherein the subject is a human.
- 15 8. The method of Claim 1, wherein for the compound of Formula I,  $R_1$  is a  $C_1$ - $C_6$  alkyl group and Ar is a substituted phenyl.
9. The method of Claim 8, wherein the substituted phenyl group is substituted with a halogen.
- 20 10. The method of Claim 1, wherein for the compound of Formula I, n is 2,  $R_1$  is a  $C_1$ - $C_6$  alkyl group and Ar is a substituted phenyl.

11. The method of Claim 10, wherein the substituted phenyl group is substituted with a halogen and  $R_1$  is a methyl group.
12. The method of Claim 1, wherein for the compound of Formula I,  $R_1$  is a  $C_1$ - $C_6$  alkyl group or a halogen and Ar is an unsubstituted phenyl.
- 5 13. The method of Claim 12, wherein  $R_2$  is hydrogen or a  $C_1$ - $C_6$  alkyl group.
14. The method of Claim 1, wherein for the compound of Formula I, n is 2,  $R_1$  is a  $C_1$ - $C_6$  alkyl group and Ar is an unsubstituted phenyl.
15. The method of Claim 14, wherein  $R_2$  is hydrogen or a  $C_1$ - $C_6$  alkyl group.
- 10 16. A method of treating nausea, vomiting, retching or any combination thereof in a subject in need thereof comprising administering to said subject a therapeutically effective amount of a compound represented by Formula II:



or a pharmaceutically acceptable salt thereof.

17. The method of Claim 16, wherein the the nausea, vomiting, retching or any combination thereof is caused by an anesthetics, radiation, a cancer chemotherapeutic agent, a toxic agent, an odor, a medicine, pregnancy or motion.
- 5 18. The method of Claim 16, wherein the nausea, vomiting, retching or any combination thereof is caused by a condition which is associated with vertigo.
19. The method of Claim 16, wherein the nausea, vomiting, retching or any combination thereof is caused by headache.
20. The method of Claim 16, wherein the nausea, vomiting, retching or any  
10 combination thereof is caused by a malady of the gastrointestinal (GI) tract.
21. The method of Claim 16, wherein the subject is a human.
22. A method for treating nausea, vomiting, retching or any combinatin thereof in a subject in need thereof comprising administering to said subject:
  - a) a first amount of a 5-HT<sub>3</sub> receptor antagonist; and
  - 15 b) a second amount of a noradrenaline reuptake inhibitorwherein the first and second amounts together comprise a therapeutically effective amount.
23. The method of Claim 22, wherein the the nausea, vomiting, retching or any  
20 combination thereof is caused by an anesthetic, radiation, a cancer chemotherapeutic agent, a toxic agent, an odor, a medicine, pregnancy or motion.

24. The method of Claim 22, wherein the medicine is selected from the group consisting of an analgesic, an antibiotic, an antifungal or a serotonin reuptake inhibitor.
25. The method of Claim 22, wherein the nausea, vomiting, retching or any combination thereof is caused by a condition which is associated with vertigo.
26. The method of Claim 22, wherein the nausea, vomiting, retching or any combination thereof is caused by headache.
27. The method of Claim 22, wherein the nausea, vomiting, retching or any combination thereof is caused by a malady of the gastrointestinal (GI) tract.
28. The method of Claim 22, wherein the subject is a human.
29. The method of Claim 22, wherein the 5-HT<sub>3</sub> receptor antagonist is selected from the group consisting of indisetron, YM-114 ((R)-2,3-dihydro-1-[(4,5,6,7-tetrahydro-1H-benzimidazol-5-yl)-carbonyl]-1H-indole), granisetron, talipexole, azasetron, bemisetron, tropisetron, ramosetron, ondansetron, palonosetron, lerisetron, alosetron, N-3389, zacopride, cilansetron, E-3620 ([3(S)-endo]-4-amino-5-chloro-N-(8-methyl-8-azabicyclo[3.2.1]-oct-3-yl-2[(1-methyl-2-butynyl)oxy]benzamide), lintopride, KAE-393, itasetron, zatoksetron, dolasetron, (±)-zacopride, (±)-renzapride, (-)-YM-060, DAU-6236, BIMU-8 and GK-128 [2-[2-methylimidazol-1-yl)methyl]-benzo[f]thiochromen-1-one monohydrochloride hemihydrate].

30. The method of Claim 29, wherein the 5-HT<sub>3</sub> receptor antagonist is selected from the group consisting of indisetron, granisetron, azasetron, bemisetron, tropisetron, ramosetron, ondansetron, palonosetron, lerisetron, alosetron, cilansetron, itasetron, zatoksetron, and dolasetron.
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31. The method of Claim 22, wherein the noradrenaline reuptake inhibitor is selected from the group consisting of venlafaxine, duloxetine, bupropion, milnacipran, reboxetine, lefepramine, desipramine, nortriptyline, tomoxetine, maprotiline, oxaprotiline, levoprotiline, viloxazine and atomoxetine.
- 10 32. The method of Claim 31, wherein the noradrenaline reuptake inhibitor is selected from the group consisting of reboxetine, lefepramine, desipramine, nortriptyline, tomoxetine, maprotiline, oxaprotiline, levoprotiline, viloxazine and atomoxetine.
- 15 33. A method for treating nausea, vomiting, retching or any combination thereof in a subject in need thereof comprising administering to said subject:
- a) a therapeutically effective amount of a 5-HT<sub>3</sub> receptor antagonist; and
  - b) a therapeutically effective amount of a noradrenaline reuptake inhibitor.
- 20 34. The method of Claim 33, wherein the the nausea, vomiting, retching or any combination thereof is caused by an anesthetic, radiation, a cancer chemotherapeutic agent, a toxic agent, an odor, a medicine, pregnancy or motion.
35. The method of Claim 33, wherein the medicine is selected from the group consisting of an analgesic, an antibiotic, an antifungal or a serotonin reuptake inhibitor.

36. The method of Claim 33, wherein the nausea, vomiting, retching or any combination thereof is caused by a condition which is associated with vertigo.
37. The method of Claim 33, wherein the nausea, vomiting, retching or any combination thereof is caused by headache.
- 5 38. The method of Claim 33, wherein the nausea, vomiting, retching or any combination thereof is caused by a malady of the gastrointestinal (GI) tract.
39. The method of Claim 33, wherein the subject is a human.
40. The method of Claim 33, wherein the 5-HT<sub>3</sub> receptor antagonist is selected from the group consisting of indisetron, YM-114 ((R)-2,3-dihydro-1-[(4,5,6,7-tetrahydro-1H-benzimidazol-5-yl)-carbonyl]-1H-indole), granisetron, talipexole, azasetron, bemesetron, tropisetron, ramosetron, ondansetron, palonosetron, lerisetron, alosetron, N-3389, zacopride, cilansetron, E-3620 ([3(S)-endo]-4-amino-5-chloro-N-(8-methyl-8-azabicyclo[3.2.1]-oct-3-yl-2[(1-methyl-2-butynyl)oxy]benzamide), lintopride, KAE-393, itasetron, zatosetron, dolasetron, 15 (±)-zacopride, (±)-renzapride, (-)-YM-060, DAU-6236, BIMU-8 and GK-128 [2-[2-methylimidazol-1-yl)methyl]-benzo[f]thiochromen-1-one monohydrochloride hemihydrate].
41. The method of Claim 40, wherein the 5-HT<sub>3</sub> receptor antagonist is selected from the group consisting of indisetron, granisetron, azasetron, bemesetron, 20 tropisetron, ramosetron, ondansetron, palonosetron, lerisetron, alosetron, cilansetron, itasetron, zatosetron, and dolasetron.

42. The method of Claim 33, wherein the noradrenaline reuptake inhibitor is selected from the group consisting of venlafaxine, duloxetine, bupropion, milnacipran, reboxetine, lefepramine, desipramine, nortriptyline, tomoxetine, maprotiline, oxaprotiline, levoprotiline, viloxazine and atomoxetine.
- 5 43. The method of Claim 42, wherein the noradrenaline reuptake inhibitor is selected from the group consisting of reboxetine, lefepramine, desipramine, nortriptyline, tomoxetine, maprotiline, oxaprotiline, levoprotiline, viloxazine and atomoxetine.
- 10 44. A method of treating nausea, vomiting, retching or any combination thereof in a subject in need thereof comprising administering to said subject a therapeutically effective amount of a noradrenaline reuptake inhibitor, wherein the noradrenaline reuptake inhibitor characterized by the substantial absence of anticholinergic effects.
- 15 45. The method of Claim 44, wherein the the nausea, vomiting, retching or any combination thereof is caused by an anesthetic, radiation, a cancer chemotherapeutic agent, a toxic agent, an odor, a medicine, pregnancy or motion.
- 20 46. The method of Claim 45, wherein the medicine is selected from the group consisting of an analgesic, an antibiotic, an antifungal or a serotonin reuptake inhibitor.
47. The method of Claim 44, wherein the nausea, vomiting, retching or any combination thereof is caused by a condition which is associated with vertigo.



48. The method of Claim 44, wherein the nausea, vomiting, retching or any combination thereof is caused by headache.
49. The method of Claim 44, wherein the nausea, vomiting, retching or any combination thereof is caused by a malady of the gastrointestinal (GI) tract.
- 5 50. The method of Claim 44, wherein the subject is a human.
51. The method of Claim 44, wherein the noradrenaline reuptake inhibitor is selected from the group consisting of venlafaxine, duloxetine, bupropion, milnacipran, reboxetine, lefepramine, desipramine, nortriptyline, tomoxetine, maprotiline, oxaprotiline, levoprotline, viloxazine and atomoxetine.
- 10 52. The method of Claim 51, wherein the noradrenaline reuptake inhibitor is selected from the group consisting of reboxetine, lefepramine, desipramine, nortriptyline, tomoxetine, maprotiline, oxaprotiline, levoprotline, viloxazine and atomoxetine.
53. A pharmaceutical composition comprising:
- 15 a) a first amount of a 5-HT<sub>3</sub> receptor antagonist; and  
b) a second amount of a noradrenaline reuptake inhibitor.
54. The pharmaceutical composition of Claim 53, further comprising a pharmaceutically acceptable carrier.
55. The pharmaceutical composition of Claim 53, wherein the 5-HT<sub>3</sub> receptor antagonist is selected from the group consisting of indisetron, YM-114 ((R)-2,3-dihydro-1-[(4,5,6,7-tetrahydro-1H-benzimidazol-5-yl)-carbonyl]-1H-indole), granisetron, talipexole, azasetron, bemesetron, tropisetron, ramosetron,
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- ondansetron, palonosetron, lerisetron, alosetron, N-3389, zacopride, cilansetron, E-3620 ([3(S)-endo]-4-amino-5-chloro-N-(8-methyl-8-azabicyclo[3.2.1]-oct-3-yl)-2[(1-methyl-2-butynyl)oxy]benzamide), lintopride, KAE-393, itasetron, zatosetron, dolasetron, ( $\pm$ )-zacopride, ( $\pm$ )-renzapride, (-)-YM-060, DAU-6236, BIMU-8 and GK-128 [2-[2-methylimidazol-1-yl)methyl]-benzo[f]thiochromen-1-one monohydrochloride hemihydrate].
56. The pharmaceutical composition of Claim 55, wherein the 5-HT<sub>3</sub> receptor antagonist is selected from the group consisting of indisetron, granisetron, azasetron, bemesetron, tropisetron, ramosetron, ondansetron, palonosetron, lerisetron, alosetron, cilansetron, itasetron, zatosetron, and dolasetron.
57. The pharmaceutical composition of Claim 53, wherein the noradrenaline reuptake inhibitor is selected from the group consisting of venlafaxine, duloxetine, bupropion, milnacipran, reboxetine, lefepramine, desipramine, nortriptyline, tomoxetine, maprotiline, oxaprotiline, levoprotline, viloxazine and atomoxetine.
58. The pharmaceutical composition of Claim 53, wherein the noradrenaline reuptake inhibitor is selected from the group consisting of reboxetine, lefepramine, desipramine, nortriptyline, tomoxetine, maprotiline, oxaprotiline, levoprotline, viloxazine and atomoxetine.
59. A method for processing a claim under a health insurance policy submitted by a claimant seeking reimbursement for costs associated with treatment of nausea, vomiting, retching or any combination thereof, wherein said treatment comprises coadministering to a subject a first amount of a 5-HT<sub>3</sub> receptor antagonist and a second amount of a noradrenaline reuptake inhibitor, wherein

the first and second amounts together comprise a therapeutically effective amount comprising:

- a) reviewing said claim;
- b) determining whether said treatment is reimbursable under said insurance policy; and
- c) processing said claim to provide partial or complete reimbursement of said costs.

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60. The method of Claim 59, wherein the nausea, vomiting, retching or any combination thereof is caused by an anesthetic, radiation, a cancer chemotherapeutic agent, a toxic agent, an odor, a medicine, pregnancy or motion.
61. The method of Claim 60, wherein the medicine is selected from the group consisting of an analgesic, an antibiotic, an antifungal or a serotonin reuptake inhibitor.
62. The method of Claim 59, wherein the nausea, vomiting, retching or any combination thereof is caused by a condition which is associated with vertigo.
63. The method of Claim 59, wherein the nausea, vomiting, retching or any combination thereof is caused by headache.
64. A method of Claim 59, wherein the nausea, vomiting, retching or any combination thereof is caused by a malady of the gastrointestinal (GI) tract.

65. A method for processing a claim under a health insurance policy submitted by a claimant seeking reimbursement for costs associated with treatment of nausea, vomiting, retching or any combination thereof, wherein said treatment comprises coadministering to a subject a therapeutically effective amount of a 5-HT<sub>3</sub> receptor antagonist and a therapeutically effective amount of a noradrenaline reuptake inhibitor comprising:
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- a) reviewing said claim;
  - b) determining whether said treatment is reimbursable under said insurance policy; and
  - 10 c) processing said claim to provide partial or complete reimbursement of said costs.
66. The method of Claim 65, wherein the nausea, vomiting, retching or any combination thereof is caused by an anesthetic, radiation, a cancer chemotherapeutic agent, a toxic agent, an odor, a medicine, pregnancy or
- 15 motion.
67. The method of Claim 66, wherein the medicine is selected from the group consisting of an analgesic, an antibiotic, an antifungal or a serotonin reuptake inhibitor.
68. The method of Claim 65, wherein the nausea, vomiting, retching or any combination thereof is caused by a condition which is associated with vertigo.
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69. The method of Claim 65, wherein the nausea, vomiting, retching or any combination thereof is caused by headache.
70. The method of Claim 65, wherein the nausea, vomiting, retching or any combination thereof is caused by a malady of the gastrointestinal (GI) tract.